

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Judi BRYANT et al.

Examiner: BALASUBRAMANIAN, Venkataraman

Serial No.: 10/722,591

Group Art Unit: 1615

Filed: November 28, 2002

Title: CHK-, PDK- AND AKT-INHIBITORY PYRIMIDINES, THEIR PRODUCTION AND USE AS PHARMACEUTICAL AGENTS

REPLY

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

SIR:

In response to the Office Communication mailed on November 2, 2007, please consider the following.

ISSUE 1:

The Office Communication alleges that the timely response filed on August 14, 2007, was not fully responsive because the section 103 rejection over Ito, US '338, was not addressed.

Applicants respectfully disagree and bring the attention of the USPTO to said response's page 23, the second and third lines under the heading "Rejections Under 35 USC 103" which reads as follows "Even the broadest definitions of the compounds in US '599, DE '650, **US '338** do not include compounds of the present claims." Emphasis added. Thus, contrary to the allegations, the response did address the rejection over US '338.

ISSUE 2:

Applicants respectfully thank the Examiner for clarifying what the terms "answers 819, 842, ..." etc. referenced in US '359. Now that applicants understand what was meant, please

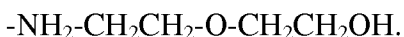
consider the following comments.

The Office Action dated April 11, 2007 alleges that answer 147 differs only in having a CF₃ at the 5-position instead of halogen, hydrogen, nitro, etc., but that because the reference teaches “5-nitro compounds,” compound 316 was pointed out, it teaches equivalency of CF₃ to nitro in the 5-position.

The above allegation / line of reasoning is contrary to strong well established law. It is not adequate for the Office Action to find several distinct compounds, e.g., various species in a reference, and combine the various substituents thereof to establish obviousness. See *In re Jones*, 958 F.2d 347, 21 U.S.P.Q. 2d 1941 (Fed. Cir. 1992) and *In re Baird*, 16 F.2d 380, 29 U.S.P.Q. 2d 1550 (Fed. Cir. 1994).

See also a recent decision of the Federal Circuit on this issue cautioning “that generalization should be avoided insofar as specific chemical structures are alleged to be prima facie obvious one from the other,” and that “in addition to structural similarity between the compounds, a prima facie case of obviousness also requires a showing of ‘adequate support in the prior art’ for the change in structure.” See *Takeda Chemical Industries Ltd. v. Alphapharm Pty. Ltd.*, 83 USPQ2d 1169 (Fed. Cir. 2007), citing *In re Grabiak*, 769 F.2d 729, 226 USPQ 870 (Fed. Cir. 1985). The changes to the structure of a compound in *Takeda* were the changing of a methyl substituent to an ethyl substituent and the changing of the position of this substituent from position 6 on a pyridyl ring of the compound to position 5 in said same ring. These changes were not found obvious from the disclosure of the prior art.

Also, note in this regard, particularly, the analysis used by the Court in *Jones*. The group at issue in *Jones* had the structure



The PTO tried to rely on the single reference's compound having two CH₂CH₂OH groups attached to a single N atom, instead of linked together as shown above. The Court stated that one could not ignore the fact that the two CH₂CH₂OH groups were not joined together to form the ether linkage-containing group required in the claim. One could not simply rely on the “-CH₂CH₂O-” features of the reference; one had to consider the entirety of the structure involved. The Patent and Trademark Office also tried to rely on a morpholino group in the single reference wherein the nitrogen atom has two ethyl groups bonded to it and linked to each other by a single

oxygen atom, thereby allegedly providing the “missing” ether oxygen noted above. Again, the Court stated that one could not ignore the entirety of the structure, i.e., the fact that this prior art group compound was cyclic. One could not apply components of its structural features in isolation apart from the group’s overall structure. Other similar analyses were rejected by the Court.

Disclosure of a particular generic formula or various species thereof with their particular set of structural components, under *Takeda, Jones* and *Baird*, does not motivate one of ordinary skill in the art to select various structural features from different compounds in isolation and apply them to other compounds.

This is especially so in a case as the present one where compounds 147 and 316 are not taught or even suggested to be equivalent, e.g., no data is provided, e.g., demonstrating similar or the same activity levels of any kind, but are merely distinct compounds identified in the same reference. The only connection between these compounds is that they are grouped within the generic formula disclosed in the reference, which generic formula defines the large number of possible substituents through nearly 20 pages. See pages 2-21 of US ‘359. Merely two compounds being within the same generic formula is inadequate under the law to provide the motivation to substitute substituents of one of its species to another one of its species. The lack of obviousness here is further enhanced by the fact that the general formula in the reference is very broad.

Additionally, compounds 147 and 316 have several structural differences, i.e., they do not only differ in the substituent in position 5, thereby providing even less motivation to one of ordinary skill in the art to consider substituting the substituent of one of these compounds to the other one of these compounds. For example, compound 147 has a –NH-CH₂-CH₂-NH-C(O)-Ph group in a position where compound 316 has a –N(Me)-CH₂-CH₂-OH group, and compound 147 has a –C(O)-NH₂ group in a position where compound 316 has a –CO-NH-CH₂-Ph group. The Office Action, for example, does not explain why one of ordinary skill in the art would find it obvious to interchange the substituents on these compounds in position 5, while not interchanging the other substituents which are also different. Thus, even under the rationale for obviousness used by the Office Action, which is not proper under the law, there are unanswered issues in the Office Action when alleging obviousness.

The Office Action, also alleges that the claimed compounds are obvious because answers 819, 842, 869, 901, 907, 910, 912, 913, 924, etc. differ from the claimed compounds in one variation. No further details are provided, e.g., what are the differences and what changes would be obvious and why are not even mentioned. For at least the same reasons as discussed above, even if there would be only one variation from the claimed compounds, which is not the case, there is no obviousness.

Nevertheless, these allegations are briefly addressed below.

Compound 819 differs from the claimed compounds in that it has a Cl group on the phenyl ring on which applicants' A and B groups are located, which groups' definition does not include Cl, and has a NO₂ group in the 5-position where applicants have a halogen group.

Compound 842 differs from the claimed compounds in that it has a CF₃ group in the 5-position where applicants have a halogen group, and has a piperidinyl group at the location of X where applicants have a -NH- group.

Likewise to compounds 819 and 842, each and every one of the compounds pointed to by the Office Action differs in at least two substituents, e.g., two, three, four, etc., from the claimed compounds.

Thus, there are at least two differences between the claimed compounds and each compound pointed to by the Office Action with no motivation for the modification of any of said compounds in any way, including in a way to achieve the claimed compounds. Thus, there is no obviousness.

Moreover, the current claims have a halogen group in the 5-position, rendering the Office Action's allegation, i.e., that a CF₃ group would have been obvious in the 5-position, moot.

Reconsideration is respectfully requested.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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